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| APPLICATION NO.                            | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.      | CONFIRMATION NO. |
|--|-------------|----------------------|--------------------------|------------------|
| 10/564,947                                 | 01/17/2006  | Margaret M. Gardner  | PU60401                  | 4064             |
| 20462                                      | 7590        | 07/01/2008           | EXAMINER                 |                  |
| SMITHKLINE BEECHAM CORPORATION             |             |                      | BARNHART, LORA ELIZABETH |                  |
| CORPORATE INTELLECTUAL PROPERTY-US, UW2220 |             |                      |                          |                  |
| P. O. BOX 1539                             |             |                      | ART UNIT                 | PAPER NUMBER     |
| KING OF PRUSSIA, PA 19406-0939             |             |                      | 1651                     |                  |
|  |             |                      |                          |                  |
|  |             |                      | NOTIFICATION DATE        | DELIVERY MODE    |
|  |             |                      | 07/01/2008               | ELECTRONIC       |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US\_cipkop@gsk.com

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/564,947             | GARDNER ET AL.      |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Lora E. Barnhart       | 1651                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 10 March 2008.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) \_\_\_\_\_ is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) 1-13 are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ .  | 6) <input type="checkbox"/> Other: _____ .                        |

## **DETAILED ACTION**

### ***Response to Amendments***

Applicant's amendments filed 4/9/08 to claim 2 have been entered. No claims have been cancelled or added. Claims 1-13 remain pending in the current application.

Upon reconsideration, the examiner has determined that a new restriction requirement is necessary in this case. This restriction requirement should replace the one mailed 3/10/08. Any inconvenience is regretted.

### ***Election/Restrictions***

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-6, drawn to a first method of using an anticoagulant to treat patients with or at risk for heparin-induced thrombocytopenia (HIT).

Group II, claim 7, drawn to a second method of using an anticoagulant to prevent an upsurge in thrombin regeneration and prevention of new thromboembolic complications in patients with or at risk for HIT.

Group III, claim 8, drawn to a third method of using an anticoagulant to lower the risk of venous limb gangrene in patients with or at risk for HIT.

Group IV, claims 9, 11, and 13, drawn to a fourth method of using an anticoagulant to lower the risk of amputation in patients with or at risk for HIT.

Group V, claims 10 and 12, drawn to a method of using argatroban and a coumarin derivative to treat patients with or at risk for HIT.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or

corresponding special technical features for the following reasons: They are not unified by a special technical feature.

The expression “special technical feature” refers to those features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. Thus, a feature found in the prior art cannot be considered to be a special technical feature.

In this case, Groups I-V are unified by the administration of an anticoagulant to a patient with or at risk for HIT until platelet counts in said patient increase. Administration of anticoagulants was known in the art at the time of the invention. Smythe et al. (2002, *American Journal of Hematology* 71: 50-52; reference u) teach administering a direct thrombin inhibitor (argatroban or lepirudin) along with warfarin to HIT patients (page 51, e.g.). Furthermore, Adkins (1998, *BioDrugs* 10: 227-255, abstract only; reference v) teaches that administration of lepirudin to HIT patients increased platelet counts in said patients (see lines 6-7 of abstract). At the time of the invention, therefore, administering anticoagulants that are thrombin inhibitors to HIT patients to increase their platelet counts was known at the time of the invention and cannot be considered a special technical feature.

An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) a product and a process specially adapted for the manufacture of said product; (2) a product and a process of use of said product; (3) a product, a process specially adapted for the manufacture of the said product, and a use of the said product; (4) a process and an apparatus or means specifically designed for carrying out the said process; or (5) a product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process. **If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims.** See 37 C.F.R. 1.475.

In this case, the application recites four different methods of using anticoagulants; the end points in claims 1 and 7-10 are distinct. Therefore, the main invention will be considered claims 1-6 only.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Anticoagulants: (a) enoxaparin, (b) dalteparin, (c) tinzaparin, (d) bivalirudin, (e) fondaparinux, (f) argatroban, (g) efegatran, (h) inogatran, (i) desirudin, and (j) lepirudin, as in claims 2, 4-6, and 10; elect ONE.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The following claim(s) are generic: claims 1, 3, 7-9, and 11-13.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Pursuant to PCT Rule 13.2 and PCT Administrative Instructions, Annex B, Part 1(f)(I)(B)(2), the species are not art-recognized equivalents.

When alternatives of chemical compounds are claimed, they shall be regarded as being of a similar nature where all alternatives have a common property or activity, and either a significant structural element is shared by all of the alternatives, or all of the alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains. The words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure

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constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together. The words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

In this case, the anticoagulants do not share a significant structural element. According to the Merck Index, 16<sup>th</sup> edition (cited in 3/10/08 Office action), argatroban is a small molecule, while bivalirudin is a synthetic polypeptide of the sequence [D-Phe-Pro-Arg-Pro-Gly-Gly-Gly-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Gly-Tyr-Leu]. Desirudin and lepirudin are derivatives of hirudin, a peptide sequence. No structure information could be found for the species efegatran and inogatran. Lepirudin and bivalirudin are peptides, while enoxaparin, dalteparin, and tinzaparin are fragments of heparin. Fondaparinux is a synthetic pentasaccharide that mimics some aspects of heparin. There is no evidence on the record that the anticoagulants in claims 2, 4-6, and 10 share a significant structural element. Therefore, inventive unity among these species is lacking.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is (571)272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/  
Primary Examiner, Art Unit 1651